## **Best Available Copy**



## SEQUENCE LISTING

Human E3 Alpha Ubiquitin Ligase Family <120> <130> 01017/35966A <140> US 09/724,126. <141> 2000-11-28 <150> US 60/187,211 <151> 1999-03-01 <160> 29 PatentIn version 3.0 <170> <210> 6308 <211> <212> DNA <213> Homo sapiens <220> <221> CDS <222> (696)..(5942) gccaagaatt cggcacgagg ggaaaagctg agcccaggaa ccaaattact tgctttacct 60 cattgtgtaa gacaagcgtc aaaaacagct tcaacctatc ttgaacaaga gaacttacct 120 ccaaaggett atcatetgte ttecaettat ccaacaaget getatggeea etgeetgtge 180 cgcacctgga accaccgcca gccccactac tgcctccact accactggtt ctcccaccct 240 gatcagctgc ttgctgctgc catcttatcc gcttctgcct gttctgagta aatgtataca 300 caccetggaa accaccatte tactttetgt gtetatgaat ttgactacte tagetggate 360 ccgagctitt ttgtacacat gtgcaagtgc ccacggggta gaatcctaaa aatagaagat 420 gtatqcaaca qttcccagca ccaaacccag atatacaacc attcagctac caaqaqctac 480 gcctgataaa ttagagggga aaaaaaaaat ctccagtccc ttcacgtcgt gacgcttgct 540 teegggaage gggeeggaag ceaeteeteg agtetgegte aaaeeegaet teaggggeeg 600 togtaaaagt gtogtocotg tototocgac oggocacagg titocgottg cetotggoog 660 713 ggggtcggca actgcaggcg tcagtttccc tcaag atg gcg gac gag gat Met Ala Asp Glu Glu Ala 761 gga ggt act gag agg atg gaa atc agc gcg gag tta ccc cag acc cct Gly Gly Thr Glu Arg Met Glu Ile Ser Ala Glu Leu Pro Gln Thr Pro 15

25

cag cgt ctg gca tct tgg tgg gat cag caa gtt gat ttt tat act gct

Gln Arg Leu Ala Ser Trp Trp Asp Gln Gln Val Asp Phe Tyr Thr Ala

3.0

809

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													gat Asp				953
													100 Gly 393				1001
													gca Ala				1049
													gtt Val				1097
													ttc Phe				1145
													gta Val				1193
													tgt Cys 180				1241
	_		_										tca Ser				1289
													gaa Glu			f	1337
cct Pro 215	gaa Glu	ctc Leu	cag Gln	ata Ile	agg Arg 220	gag Glu	aaa Lys	aat Asn	gaa Glu	aga Arg 225	tac Tyr	tat Tyr	tgt Cys	gtc Val	ctt Leu 230		1385
													agc Ser				1433
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tgc Cys	cag Gln 280	gaa Glu	gca Ala	aag Lys	gaa Glu	gat Asp 285	ata Ile	aag Lys	agt Ser	cat His	tca Ser 290	gaa Glu	aat Asn	gtc Val	tct Ser	1577
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					cgt Arg											1673
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					gaa Glu	_		_	_	_			_			2201
					att Ile											2249

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	ata cag ato Ile Gln Met 540	Gln Leu					2345
	gct tgt gat Ala Cys Asp 555						2393
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	gta caa tog Val Gln Sei						2489
	gag gat ctt Glu Asp Let	_		_		J J	2537
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_	ggt gca tct Gly Ala Sen 700	Leu Met	_	-	_	-	2825
	g agg tat gaa n Arg Tyr Gli 715						2873
	cag gat ttg Gln Asp Let 730	lle Lys					2921
atg ctt cag Met Leu Glr 745	ggtc ctc ato Val Leu Ile	tat att of Tyr Ile 7	gtg ggt Val Gly	gag cgt Glu Arg	tat gta Tyr Val 755	cct gga Pro Gly	2969

				aaa Lys										3017
_	_		_	ccc Pro 780	_			_	_		_			3065
				aat Asn										3113
				aaa Lys										3161
		_		ctg Leu		_			_					3209
		_		agc Ser	_				_	_	_		_	3257
	_			gat Asp 860	_	_	_	_					_	3305
				agc Ser										3353
				agg Arg										3401
				gaa Glu										3449
				gaa Glu										3497
				gac Asp 940										3545
				caa Gln										3593
				aag Lys										3641
_		_	-	tta Leu	_	-			_			 _		3689

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cmit

-	gct Ala 1225		_			_		_				Ile	_		4409
	ctg Leu 1240														4454
	aac Asn 1255					ttc Phe 1260									4499
	ttg Leu 1270						_	_			_			_	45 <b>4</b> 4
	aaa Lys 1285														4589
	aca Thr 1300					gga Gly 1305	Leu								4634
_	cct Pro 1315	_	_		_	_			_		_	_			4679
atc Ile	cag Gln 1330	gca Ala	att Ile	gaa Glu	aat Asn	cta Leu 1335	ttg Leu	gga Gly	gat Asp	gaa Glu	gga Gly 1340	aaa Lys	cct Pro	ctg Leu	4724
	gga Gly 1345														4769
	cag Gln 1360														4814
	cag Gln 1375												cct Pro		4859
	aaa Lys 1390	Ser	_	_			_		_			_	_		4904
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_	gac Asp 1420			_	_	_				_	_		tcc Ser		4994
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ggc tgg Gly Trr 149	Tyr											cct Pro		5219
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gca cto Ala Leu 154	Cys									ttg Leu 1550		ctg Leu		5354
ttc cac Phe Glr 155	Glu													5399
tgt gca Cys Ala 157	Āsp						_	_	_	caa Gln 1580				5444
gtg gtc Val Val 158	Arg			_	aaa Lys 1590	_				ata Ile 1595				5489
gat gad Asp Asp 160	Tyr				ctg Leu 1605								tgc Cys	5534
eca egg Pro Arg 161	Ser				gag Glu 1620									5579
ttc tgt Phe Cys 163	Gly									tgc Cys 1640				5624
att gtg Ile Val 164	Asr				gtt Val 1650									5669
cac tgt His Cys 166	Gly				tgc Cys 1665									5714

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cat ttg gtc tgg caa caa cac tgc att ata gaa gag att gct agg His Leu Val Trp Gln Gln His Cys Ile Ile Glu Glu Ile Ala Arg 1720 1725 1730	5894
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Glu Ile Tyr Phe Ala Glu Met Asp Pro Asp Leu Glu Lys Gln Glu Glu 50 55 60	
Ser Val Gln Met Ser Ile Phe Thr Pro Leu Glu Trp Tyr Leu Phe Gly	
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Gln Leu Cys Gly Arg Val Phe Lys Ser Gly Glu Thr Thr Tyr Ser Cys 100 105 110

Arg Asp Cys Ala Ile Asp Pro Thr Cys Val Leu Cys Met Asp Cys Phe 120 Gln Asp Ser Val His Lys Asn His Arg Tyr Lys Met His Thr Ser Thr Gly Gly Gly Phe Cys Asp Cys Gly Asp Thr Glu Ala Trp Lys Thr Gly Pro Phe Cys Val Asn His Glu Pro Gly Arg Ala Gly Thr Ile Lys Glu Asn Ser Arg Cys Pro Leu Asn Glu Glu Val Ile Val Gln Ala Arg Lys 185 Ile Phe Pro Ser Val Ile Lys Tyr Val Val Glu Met Thr Ile Trp Glu Glu Glu Lys Glu Leu Pro Pro Glu Leu Gln Ile Arg Glu Lys Asn Glu 215 Arg Tyr Tyr Cys Val Leu Phe Asn Asp Glu His His Ser Tyr Asp His Val Ile Tyr Ser Leu Gln Arg Ala Leu Asp Cys Glu Leu Ala Glu Ala Gln Leu His Thr Thr Ala Ile Asp Lys Glu Gly Arg Arg Ala Val Lys Ala Gly Ala Tyr Ala Ala Cys Gln Glu Ala Lys Glu Asp Ile Lys Ser His Ser Glu Asn Val Ser Gln His Pro Leu His Val Glu Val Leu His 295 Ser Glu Ile Met Ala His Gln Lys Phe Ala Leu Arg Leu Gly Ser Trp Met Asn Lys Ile Met Ser Tyr Ser Ser Asp Phe Arg Gln Ile Phe Cys 325 Gln Ala Cys Leu Arg Glu Glu Pro Asp Ser Glu Asn Pro Cys Leu Ile 345 Ser Arg Leu Met Leu Trp Asp Ala Lys Leu Tyr Lys Gly Ala Arg Lys 355 Ile Leu His Glu Leu Ile Phe Ser Ser Phe Phe Met Glu Met Glu Tyr 370 375 Lys Lys Leu Phe Ala Met Glu Phe Val Lys Tyr Tyr Lys Gln Leu Gln Lys Glu Tyr Ile Ser Asp Asp His Asp Arg Ser Ile Ser Ile Thr Ala Leu Ser Val Gln Met Phe Thr Val Pro Thr Leu Ala Arg His Leu Ile 425 Glu Glu Gln Asn Val Ile Ser Val Ile Thr Glu Thr Leu Leu Glu Val 440 435 445

Leu Pro Glu Tyr Leu Asp Arg Asn Asn Lys Phe Asn Phe Gln Gly Tyr 450

Ser Gln Asp Lys Leu Gly Arg Val Tyr Ala Val Ile Cys Asp Leu Lys 465

Tyr Ile Leu Ile Ser Lys Pro Thr Ile Trp Thr Glu Arg Leu Arg Met 495

Gln Phe Leu Glu Gly Phe Arg Ser Phe Leu Lys Ile Leu Thr Cys Met 500 505 510

Gln Gly Met Glu Glu Ile Arg Arg Gln Val Gly Gln His Ile Glu Val 515 520 525

Asp Pro Asp Trp Glu Ala Ala Ile Ala Ile Gln Met Gln Leu Lys Asn 530 540

Ile Leu Leu Met Phe Gln Glu Trp Cys Ala Cys Asp Glu Glu Leu Leu 545 550 555 560

Leu Val Ala Tyr Lys Glu Cys His Lys Ala Val Met Arg Cys Ser Thr 565 570 575

Ser Phe Ile Ser Ser Ser Lys Thr Val Val Gln Ser Cys Gly His Ser 580 585 590

Leu Glu Thr Lys Ser Tyr Arg Val Ser Glu Asp Leu Val Ser Ile His 595 600 605

Leu Pro Leu Ser Arg Thr Leu Ala Gly Leu His Val Arg Leu Ser Arg 610 620

Leu Gly Ala Val Ser Arg Leu His Glu Phe Val Ser Phe Glu Asp Phe 625 630 635 640

Gln Val Glu Val Leu Val Glu Tyr Pro Leu Arg Cys Leu Val Leu Val
645 650 655

Ala Gln Val Val Ala Glu Met Trp Arg Arg Asn Gly Leu Ser Leu Ile 660 665 670

Ser Gln Val Phe Tyr Tyr Gln Asp Val Lys Cys Arg Glu Glu Met Tyr 675 680 685

Asp Lys Asp Ile Ile Met Leu Gln Ile Gly Ala Ser Leu Met Asp Pro 690 695 700

Asn Lys Phe Leu Leu Leu Val Leu Gln Arg Tyr Glu Leu Ala Glu Ala 705 710 715 720

Phe Asn Lys Thr Ile Ser Thr Lys Asp Gln Asp Leu Ile Lys Gln Tyr
725 730 735

Asn Thr Leu Ile Glu Glu Met Leu Gln Val Leu Ile Tyr Ile Val Gly
740 745 750

Glu Arg Tyr Val Pro Gly Val Gly Asn Val Thr Lys Glu Glu Val Thr 755 760 765

Al crit

Glu A
Gly A
Met 4
Pro 865

Met Arg Glu Ile Ile His Leu Leu Cys Ile Glu Pro Met Pro His Ser 770 775 780

Ala Ile Ala Lys Asn Leu Pro Glu Asn Glu Asn Asn Glu Thr Gly Leu 785

785 790 795 800

Glu Asn Val Ile Asn Lys Val Ala Thr Phe Lys Lys Pro Gly Val Ser 805 810 815

Gly His Gly Val Tyr Glu Leu Lys Asp Glu Ser Leu Lys Asp Phe Asn 820 825 830

Met Tyr Phe Tyr His Tyr Ser Lys Thr Gln His Ser Lys Ala Glu His 835 840 845

Met Gln Lys Lys Arg Arg Lys Gln Glu Asn Lys Asp Glu Ala Leu Pro 850 860

Pro Pro Pro Pro Glu Phe Cys Pro Ala Phe Ser Lys Val Ile Asn 865 870 875 885

Leu Leu Asn Cys Asp Ile Met Met Tyr Ile Leu Arg Thr Val Phe Glu 885 890 895

Arg Ala Ile Asp Thr Asp Ser Asn Leu Trp Thr Glu Gly Met Leu Gln 900 905 910

Met Ala Phe His Ile Leu Ala Leu Gly Leu Leu Glu Glu Lys Gln Gln 915 920 925

Leu Gln Lys Ala Pro Glu Glu Glu Val Thr Phe Asp Phe Tyr His Lys 930 935 940

Ala Ser Arg Leu Gly Ser Ser Ala Met Asn Ile Gln Met Leu Leu Glu 945 950 955 960

Lys Leu Lys Gly Ile Pro Gln Leu Glu Gly Gln Lys Asp Met Ile Thr 965 970 975

Trp Ile Leu Gln Met Phe Asp Thr Val Lys Arg Leu Arg Glu Lys Ser 980 985 990

Cys Leu Ile Val Ala Thr Thr Ser Gly Ser Glu Ser Ile Lys Asn Asp 995 1000 1005

Glu Ile Thr His Asp Lys Glu Lys Ala Glu Arg Lys Arg Lys Ala 1010 1015 1020

Glu Ala Ala Arg Leu His Arg Gln Lys Ile Met Ala Gln Met Ser 1025 1030 1035

Ala Leu Gln Lys Asn Phe Ile Glu Thr His Lys Leu Met Tyr Asp 1040 1045 1050

Asn Thr Ser Glu Met Pro Gly Lys Glu Asp Ser Ile Met Glu Glu 1055 1060 1065

Glu Ser Thr Pro Ala Val Ser Asp Tyr Ser Arg Ile Ala Leu Gly
1070 1080

Pro Lys Arg Gly Pro Ser Val Thr Glu Lys Glu Val Leu Thr Cys 1085 1090 1095 Ile Leu Cys Gln Glu Glu Gln Glu Val Lys Ile Glu Asn Asn Ala Met Val Leu Ser Ala Cys Val Gln Lys Ser Thr Ala Leu Thr Gln 1120 1115 His Arg Gly Lys Pro Ile Glu Leu Ser Gly Glu Ala Leu Asp Pro 1130 1135 Leu Phe Met Asp Pro Asp Leu Ala Tyr Gly Thr Tyr Thr Gly Ser 1150 1145 Cys Gly His Val Met His Ala Val Cys Trp Gln Lys Tyr Phe Glu 1165 Ala Val Gln Leu Ser Ser Gln Gln Arg Ile His Val Asp Leu Phe Asp Leu Glu Ser Gly Glu Tyr Leu Cys Pro Leu Cys Lys Ser Leu 1190 1195 1200 Cys Asn Thr Val Ile Pro Ile Ile Pro Leu Gln Pro Gln Lys Ile Asn Ser Glu Asn Ala Asp Ala Leu Ala Gln Leu Leu Thr Leu Ala 1220 1225 Arg Trp Ile Gln Thr Val Leu Ala Arg Ile Ser Gly Tyr Asn Ile 1235 1240 Arg His Ala Lys Gly Glu Asn Pro Ile Pro Ile Phe Phe Asn Gln 1250. Gly Met Gly Asp Ser Thr Leu Glu Phe His Ser Ile Leu Ser Phe 1270 Gly Val Glu Ser Ser Ile Lys Tyr Ser Asn Ser Ile Lys Glu Met 1280 1285 1290 Val Ile Leu Phe Ala Thr Thr Ile Tyr Arg Ile Gly Leu Lys Val 1300 1305 Pro Pro Asp Glu Arg Asp Pro Arg Val Pro Met Leu Thr Trp Ser 1315 Thr Cys Ala Phe Thr Ile Gln Ala Ile Glu Asn Leu Leu Gly Asp 1325 Glu Gly Lys Pro Leu Phe Gly Ala Leu Gln Asn Arg Gln His Asn 1345 1350 Gly Leu Lys Ala Leu Met Gln Phe Ala Val Ala Gln Arg Ile Thr Cys Pro Gln Val Leu Ile Gln Lys His Leu Val Arg Leu Leu Ser 1375 Val Val Leu Pro Asn Ile Lys Ser Glu Asp Thr Pro Cys Leu Leu 1385 1390 1395 Ser Ile Asp Leu Phe His Val Leu Val Gly Ala Val Leu Ala Phe 1400 1405 1410

The the

Pro Ser Leu Tyr Trp Asp Asp Pro Val Asp Leu Gln Pro Ser Ser 1420 1415 Val Ser Ser Ser Tyr Asn His Leu Tyr Leu Phe His Leu Ile Thr Met Ala His Met Leu Gln Ile Leu Leu Thr Val Asp Thr Gly Leu 1450 Pro Leu Ala Gln Val Gln Glu Asp Ser Glu Glu Ala His Ser Ala 1460 1465 Ser Ser Phe Phe Ala Glu Ile Ser Gln Tyr Thr Ser Gly Ser Ile 1475 Gly Cys Asp Ile Pro Gly Trp Tyr Leu Trp Val Ser Leu Lys Asn Gly Ile Thr Pro Tyr Leu Arg Cys Ala Ala Leu Phe Phe His Tyr 1505 1510 1515 Leu Leu Gly Val Thr Pro Pro Glu Glu Leu His Thr Asn Ser Ala 1525 Glu Gly Glu Tyr Ser Ala Leu Cys Ser Tyr Leu Ser Leu Pro Thr 1535 1540 Asn Leu Phe Leu Leu Phe Gln Glu Tyr Trp Asp Thr Val Arg Pro 1550 1555 1560 Leu Leu Gln Arg Trp Cys Ala Asp Pro Ala Leu Leu Asn Cys Leu 1570 Lys Gln Lys Asn Thr Val Val Arg Tyr Pro Arg Lys Arg Asn Ser Leu Ile Glu Leu Pro Asp Asp Tyr Ser Cys Leu Leu Asn Gln Ala 1595 1600 1605 Ser His Phe Arg Cys Pro Arg Ser Ala Asp Asp Glu Arg Lys His 1610 1615 Pro Val Leu Cys Leu Phe Cys Gly Ala Ile Leu Cys Ser Gln Asn 1630 1625 Ile Cys Cys Gln Glu Ile Val Asn Gly Glu Glu Val Gly Ala Cys 1640 1645 1650 Ile Phe His Ala Leu His Cys Gly Ala Gly Val Cys Ile Phe Leu 1660 Lys Ile Arg Glu Cys Arg Val Val Leu Val Glu Gly Lys Ala Arg 1670 1675 Gly Cys Ala Tyr Pro Ala Pro Tyr Leu Asp Glu Tyr Gly Glu Thr Asp Pro Gly Leu Lys Arg Gly Asn Pro Leu His Leu Ser Arg Glu 1700 1705 1710

A 1



Arg Tyr Arg Lys Leu His Leu Val Trp Gln Gln His Cys Ile Ile 1715 1720 Glu Glu Ile Ala Arg Ser Gln Glu Thr Asn Gln Met Leu Phe Gly 1730 Phe Asn Trp Gln Leu Leu 1745 <210> 3 <211> 6300 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (295)..(5559) <400> gccaagaatt cggcacgagg tgtcaggcct ggggttttct gtgtccttcc ctgggtcagg 60 gacgagccag tgacttgact cttgggcgct aagcttggga gggagcgcag gaggccgctg 120 tectteettt eeggtteaeg teaecettet etecetetgt tgeteeaeet geageeaett 180 ggacggetee gggactgatt geetggggea ggggtggeag tegaggeege eggggeegag 240 gtgaggetge ageteteegg geggeggtag egetggggag gaggaggaga gaag atg 297 Met geg teg gag eta gag eca gag gtg eag gee ate gae egg agt ttg etg 345 Ala Ser Glu Leu Glu Pro Glu Val Gln Ala Ile Asp Arq Ser Leu Leu gaa tgt tcg gcc gag gag att gcg ggg aaa tgg ctg caa gca act gac 393 Glu Cys Ser Ala Glu Glu Ile Ala Gly Lys Trp Leu Gln Ala Thr Asp 20 ctc act aga gaa gtg tac cag cat tta gcc cac tat gta ccc aaa atc 441 Leu Thr Arg Glu Val Tyr Gln His Leu Ala His Tyr Val Pro Lys Ile tac tgc agg ggt ccc aac cct ttt cca cag aaa gaa gac atg ctg gca 489 Tyr Cys Arg Gly Pro Asn Pro Phe Pro Gln Lys Glu Asp Met Leu Ala cag cat gtt ttg ttg gga cca atg gaa tgg tac ctt tgt ggt gaa gat 537 Gln His Val Leu Leu Gly Pro Met Glu Trp Tyr Leu Cys Gly Glu Asp 70 cct gca ttt gga ttt cca aaa ctt gag caa gca aac aaa cct tct cat 585 Pro Ala Phe Gly Phe Pro Lys Leu Glu Gln Ala Asn Lys Pro Ser His ctt tgt ggt cgt gtt ttt aaa gta gga gag cct aca tat tct tgc aga 633

125

681

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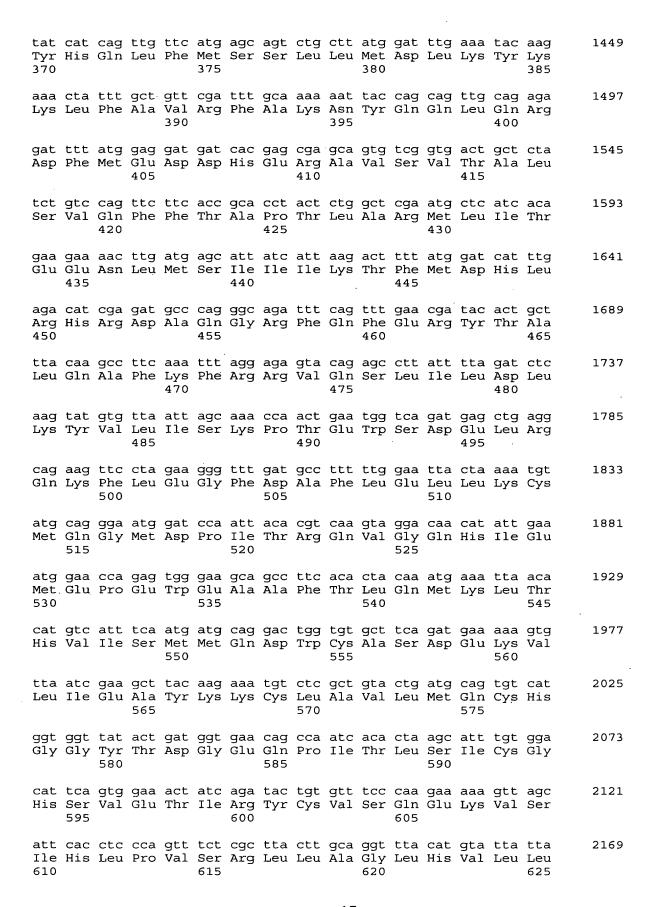
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Asp Cys Ala Val Asp Pro Thr Cys Val Leu Cys Met Glu Cys Phe Leu

120

							cga Arg									729
gga Gly	ggt Gly	ttc Phe	tgt Cys	gac Asp 150	tgt Cys	ggt Gly	gat Asp	act Thr	gaa Glu 155	gcc Ala	tgg Trp	aaa Lys	gag Glu	ggt Gly 160	cct Pro	777
							aac Asn									825
							gaa Glu 185									873
							tat Tyr									921
	Ğlu						gat Asp									969
							aat Asn									1017
							gct Ala									1065
							gat Asp 265									1113
							gag Glu									1161
							cca Pro									1209
							ttt Phe									1257
							gat Asp									1305
							gat Asp 345									1353
							aaa Lys									1401

Al cont



HI, t

	aaa Lys															2217
_	ctt Leu	_			_	_		_				_	_		_	2265
	tgt Cys															2313
	gta Val 675															2361
	ttt Phe															2409
	cca Pro															2457
	att Ile															2505
	cat His	_	_	_	_	_	_						_	_	_	2553
•																
	tac Tyr 755															2601
Leu gga	Tyr	Leu gta	Ile	Ile gct	Met	Leu 760 gat	Val gaa	Gly	Glu aag	Arg cga	Phe 765 gag	Ser	Pro	Gly	Val cag	2601 2649
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att Ile 1535					aca Thr 1540						_	agc Ser	4941

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cag Gln 1745					att Ile 1750						taat	tatt	egc		5569
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Pro Tyr Cys Gln Lys His Glu Leu Asn Thr Ser Glu Ile Glu Glu Glu 165 170 175

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Gln Val Ile Tyr Thr Leu Gln Lys Ala Val Asn Cys Thr Gln Lys Glu 245 250 255

Ala Ile Gly Phe Ala Thr Thr Val Asp Arg Asp Gly Arg Arg Ser Val 260 265 270

Arg Tyr Gly Asp Phe Gln Tyr Cys Glu Gln Ala Lys Ser Val Ile Val 275 280 285

Arg Asn Thr Ser Arg Gln Thr Lys Pro Leu Lys Val Gln Val Met His 290 295 300

Ser Ser Ile Val Ala His Gln Asn Phe Gly Leu Lys Leu Leu Ser Trp 305 310 315 320

Leu Gly Ser Ile Ile Gly Tyr Ser Asp Gly Leu Arg Arg Ile Leu Cys 325 330 335

Gln Val Gly Leu Gln Glu Gly Pro Asp Gly Glu Asn'Ser Ser Leu Val 340 345 350

Asp Arg Leu Met Leu Ser Asp Ser Lys Leu Trp Lys Gly Ala Arg Ser 355 360 365

Val Tyr His Gln Leu Phe Met Ser Ser Leu Leu Met Asp Leu Lys Tyr 370 375 380

Lys Lys Leu Phe Ala Val Arg Phe Ala Lys Asn Tyr Gln Gln Leu Gln 385 390 395 400

Arg Asp Phe Met Glu Asp Asp His Glu Arg Ala Val Ser Val Thr Ala 405 410 415

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Thr Glu Glu Asn Leu Met Ser Ile Ile Ile Lys Thr Phe Met Asp His 435 440 445

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Leu Lys Tyr Val Leu Ile Ser Lys Pro Thr Glu Trp Ser Asp Glu Leu 485 490 495

Arg Gln Lys Phe Leu Glu Gly Phe Asp Ala Phe Leu Glu Leu Lys 500 505 510

Cys Met Gln Gly Met Asp Pro Ile Thr Arg Gln Val Gly Gln His Ile 515 520 525 Glu Met Glu Pro Glu Trp Glu Ala Ala Phe Thr Leu Gln Met Lys Leu 530

Thr His Val Ile Ser Met Met Gln Asp Trp Cys Ala Ser Asp Glu Lys 545

Val Leu Ile Glu Ala Tyr Lys Lys Cys Leu Ala Val Leu Met Gln Cys
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His Gly Gly Tyr Thr Asp Gly Glu Gln Pro Ile Thr Leu Ser Ile Cys
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Ser Ile His Leu Pro Val Ser Arg Leu Leu Ala Gly Leu His Val Leu 610 615 620

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Ser Glu Leu Ser Pro Pro Met Leu Ile Glu His Pro Leu Arg Cys Leu 645 650 655

Val Leu Cys Ala Gln Val His Ala Gly Met Trp Arg Arg Asn Gly Phe 660 665 670

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- Glu His Val Val Thr Phe Thr Phe Thr Gln Lys Ile Ser Lys Pro Gly 945 950 955 960
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Ile Tyr Cys Arg Gly Pro Asn Pro Phe Pro Gln Lys Glu Asp Thr Leu 50 55 60

Ala Gln His Ile Leu Leu Gly Pro Met Glu Trp Tyr Ile Cys Ala Glu 65 . 70 75 80

Asp Pro Ala Leu Gly Phe Pro Lys Leu Glu Gln Ala Asn Lys Pro Ser 85 90 95

His Leu Cys Gly Arg Val Phe Lys Val Gly Glu Pro Thr Tyr Ser Cys
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Arg Asp Cys Ala Val Asp Pro Thr Cys Val Leu Cys Met Glu Cys Phe 115 120 125

Leu Gly Ser Ile His Arg Asp His Arg Tyr Arg Met Thr Thr Ser Gly 130 135 140

Gly Gly Gly Phe Cys Asp Cys Gly Asp Thr Glu Ala Trp Lys Glu Gly 145 150 155 160

Pro Tyr Cys Gln Lys His Lys Leu Ser Ser Ser Glu Val Val Glu Glu 165 170 175

Glu Asp Pro Leu Val His Leu Ser Glu Asp Val Ile Ala Arg Thr Tyr 180 185 190

Asn Ile Phe Ala Ile Met Phe Arg Tyr Ala Val Asp Ile Leu Thr Trp 195 200 205

Glu Lys Glu Ser Glu Leu Pro Glu Asp Leu Glu Val Ala Glu Lys Ser 210 215 220 Asp Thr Tyr Tyr Cys Met Leu Phe Asn Asp Glu Val His Thr Tyr Glu 230 235 Gln Val Ile Tyr Thr Leu Gln Lys Ala Val Asn Cys Thr Gln Lys Glu Ala Ile Gly Phe Ala Thr Thr Val Asp Arg Asp Gly Arg Arg Pro Val Arg Tyr Gly Asp Phe Gln Tyr Cys Asp Gln Ala Lys Thr Val Ile Val Arg Asn Thr Ser Arg Gln Thr Lys Pro Leu Lys Val Gln Val Met His 295 Ser Ser Val Ala Ala His Gln Asn Phe Gly Leu Lys Ala Leu Ser Trp Leu Gly Ser Val Ile Gly Tyr Ser Asp Gly Leu Arg Arg Ile Leu Cys 330 Gln Val Gly Leu Gln Glu Gly Pro Asp Gly Glu Asn Ser Ser Leu Val Asp Arg Leu Met Leu Asn Asp Ser Lys Leu Trp Lys Gly Ala Arg Ser Val Tyr His Gln Leu Phe Met Ser Ser Leu Leu Met Asp Leu Lys Tyr .375 Lys Lys Leu Phe Ala Leu Arg Phe Ala Lys Asn Tyr Arg Gln Leu Gln 395 Arg Asp Phe Met Glu Asp Asp His Glu Arg Ala Val Ser Val Thr Ala Leu Ser Val Gln Phe Phe Thr Ala Pro Thr Leu Ala Arg Met Leu Leu 425 Thr Glu Glu Asn Leu Met Thr Val Ile Ile Lys Ala Phe Met Asp His Leu Lys His Arg Asp Ala Gln Gly Arg Phe Gln Phe Glu Arg Tyr Thr 455 Ala Leu Gln Ala Phe Lys Phe Arg Arg Val Gln Ser Leu Ile Leu Asp 475 Leu Lys Tyr Val Leu Ile Ser Lys Pro Thr Glu Trp Ser Asp Glu Leu 490 Arg Gln Lys Phe Leu Gln Gly Phe Asp Ala Phe Leu Glu Leu Lys 505 Cys Met Gln Gly Met Asp Pro Ile Thr Arg Gln Val Gly Gln His Ile Glu Met Glu Pro Glu Trp Glu Ala Ala Phe Thr Leu Gln Met Lys Leu 530 535 540

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- Phe Cys Pro Leu Phe Ala Ser Leu Val Asn Ile Leu Gln Cys Asp Val 885 890 895
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- Gly Ser Ala Trp Ser Glu Ser Met Leu Gln Arg Val Leu His Leu Ile 915 920 925
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Ser	Asp 1400	Ser	Tyr	Glu	Asp	Leu 1405	Pro	Cys	Ile	Leu	Asp 1410	Ile	Asp	Met
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Cys	Gln 1430	_	Phe	Ser	Gly	Ser 1435	Ser	Leu	Ala	Thr	Gly 1440	Asp	Leu	His
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Gln	Tyr 1490		Gly	Ser	Ala	Leù 1495	Lys	Glu	Ala	Pro	Ser 1500	Gly	Trp	His
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Pro Phe Cys Val Asp His Glu Pro Gly Arg Ala Gly Thr Thr Lys Glu 165 170 Ser Leu His Cys Pro Leu Asn Glu Glu Val Ile Ala Gln Ala Arg Arg Ile Phe Pro Ser Val Ile Lys Tyr Ile Val Glu Met Thr Ile Trp Glu Glu Glu Lys Glu Leu Pro Pro Glu Leu Gln Ile Arg Glu Lys Asn Glu 215 Arg Tyr Tyr Cys Val Leu Phe Asn Asp Glu His His Ser Tyr Asp His Val Ile Tyr Ser Leu Gln Arg Ala Leu Asp Cys Glu Leu Ala Glu Ala Gln Leu His Thr Thr Ala Ile Asp Lys Glu Gly Arg Arg Ala Val Lys 265 Ala Gly Val Tyr Ala Thr Cys Gln Glu Ala Lys Glu Asp Ile Lys Ser His Ser Glu Asn Val Ser Gln His Pro Leu His Val Glu Val Leu His 295 Ser Val Val Met Ala His Gln Lys Phe Ala Leu Arg Leu Gly Ser Trp 310 Met Asn Lys Ile Met Ser Tyr Ser Ser Asp Phe Arg Gln Ile Phe Cys 325 Gln Ala Cys Leu Val Glu Glu Pro Gly Ser Glu Asn Pro Cys Leu Ile 345 Ser Arg Leu Met Leu Trp Asp Ala Lys Leu Tyr Lys Gly Ala Arg Lys Ile Leu His Glu Leu Ile Phe Ser Ser Phe Phe Met Glu Met Glu Tyr 375 Lys Lys Leu Phe Ala Met Glu Phe Val Lys Tyr Tyr Lys Gln Leu Gln 390 Lys Glu Tyr Ile Ser Asp Asp His Glu Arg Ser Ile Ser Ile Thr Ala Leu Ser Val Gln Met Leu Thr Val Pro Thr Leu Ala Arg His Leu Ile 425 Glu Glu Gln Asn Val Ile Ser Val Ile Thr Glu Thr Leu Leu Glu Val Leu Pro Glu Tyr Leu Asp Arg Asn Asn Lys Phe Asn Phe Gln Gly Tyr 455 Ser Gln Asp Lys Leu Gly Arg Val Tyr Ala Val Ile Cys Asp Leu Lys Tyr Ile Leu Ile Ser Lys Pro Val Ile Trp Thr Glu Arg Leu Arg Ala 490

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- Pro Pro Pro Pro Glu Phe Cys Pro Ala Phe Ser Lys Val Val Asn 865 870 875 886
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Trp Tyr Leu Phe Gly Glu Asp Pro Asp Ile Cys Leu Glu Lys Leu Lys 85 90 95

His Ser Gly Ala Phe Gln Leu Cys Gly Arg Val Phe Lys Ser Gly Glu 100 105 110

Thr Thr Tyr Ser Cys Arg Asp Cys Ala Ile Asp Pro Thr Cys Val Leu 115 120 125

Cys Met Asp Cys Phe Gln Asp Ser Val His Lys Asn His Arg Tyr Lys 130 135 140

Met His Thr Ser Thr Gly Gly Gly Phe Cys Asp Cys Gly Asp Thr Glu 145 150 155 160

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